



HEPATITIS C February 2003

1: AIDS Read 2002 Dec;12(12):527-35

Comment in:

AIDS Read. 2002 Dec;12(12):530-1.

Strategies to improve access to sterile syringes for injection drug users.

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The high prevalence of infection with HIV and other blood-borne pathogens in injection drug users (IDUs) is directly related to the lack of syringe access. Needle exchange programs (NEPs), syringe prescription, and syringe deregulation are 3 approaches to increasing access to sterile syringes for IDUs. The benefits of NEPs have been repeatedly demonstrated, but the impact of NEPs has been limited by a lack of federal funding. Syringe prescription for IDUs is a promising new strategy supported by many organizations; legalizing syringe purchase and possession has led to a substantial improvement in syringe access in many states. Because each approach has unique advantages, providing IDUs with a variety of options for syringe access is likely to be most beneficial.

PMID: 12518719 [PubMed - indexed for MEDLINE]

2: Am J Phys Med Rehabil 2003 Jan;82(1):28-32

Serologic examinations of hepatitis, cytomegalovirus, and rubella in patients with Bell's palsy.

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OBJECTIVE: The aim of this retrospective case review was to investigate serologic evidence of cytomegalovirus, rubella virus, and hepatitis A, B, and C viruses in patients with Bell's palsy. **DESIGN:** A total of 24 patients with idiopathic facial paralysis, without a history of trauma, any evidence of a tumor on high-resolution computed tomographic imaging, or any otologic disease, and 33 healthy individuals as a control group were included in this study. Facial paralysis of the patient was evaluated with the House-Brackmann grading scale. Specific immunoglobulin G and M titers were determined for cytomegalovirus, rubella, hepatitis A, hepatitis B, and hepatitis C by enzyme-linked immunosorbent assay. **RESULTS:** Serologic positivity for hepatitis B was found in 15 of 21 Bell's palsy patients, compared with 32.1% in the control group. The difference was statistically significant. There was no difference in the prevalence of serologic positivity for cytomegalovirus, hepatitis A, and rubella between the patient and control groups. In one Bell's palsy patient, serologic evidence of recent cytomegalovirus infection was indicated by changes in antibody titers between samples taken on presentation and on the 16th day. There was no

serologic evidence of hepatitis C in either Bell's palsy patients or the control group.
CONCLUSION: There seems to be an association between hepatitis B and idiopathic facial paralysis. In addition, cytomegalovirus might contribute to the development of Bell's palsy in some cases with Bell's palsy. Further studies are required to confirm these data.

PMID: 12510182 [PubMed - indexed for MEDLINE]

3: Am J Psychiatry 2003 Jan;160(1):172-4

Prevalence of hepatitis C among psychiatric patients in the public sector.

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OBJECTIVE: This study estimated the seroprevalence of hepatitis C virus in a public-sector psychiatric hospital. METHOD: Patients admitted between Jan. 1, 1998, and Dec. 30, 2000, were routinely screened for hepatitis C virus antibody on admission. RESULTS: A total of 133 (8.5%) of 1,556 patients admitted were positive for the hepatitis C virus. Aminotransferase levels were elevated but rarely abnormal among patients positive for the hepatitis C virus. Hepatitis B surface antibody was found in 27.8% of the patients positive for the hepatitis C virus. These patients were more likely to receive a diagnosis of psychoactive substance use disorder but no other psychiatric diagnoses. CONCLUSIONS: The prevalence of hepatitis C virus is high among psychiatric patients in the public sector. Much needs to be learned about the role of universal screening and effective techniques for primary prevention and antiviral treatment in this population.

PMID: 12505819 [PubMed - indexed for MEDLINE]

4: Am J Psychiatry 2003 Jan;160(1):174-8

The safety of valproic acid use for patients with hepatitis C infection.

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OBJECTIVE: Valproic acid is frequently not recommended for patients with hepatic dysfunction. The authors evaluated the association between hepatitis C and alanine aminotransferase (ALT) values during valproic acid treatment. METHOD: ALT changes in 564 individuals beginning valproic acid treatment were examined. Changes among those with positive hepatitis C status were compared with changes among patients with positive hepatitis C status who were taking other psychotropic agents. RESULTS: ALT elevations with valproic acid were significantly greater among patients with positive hepatitis C status than those with negative or unknown status. Among patients with positive hepatitis C status, ALT increases did not differ significantly between valproic acid and other medications. CONCLUSIONS: Use of valproic acid may be possible for some patients with hepatitis C. ALT increases in seropositive patients may be partially related to chronic hepatitis infection. However, ALT levels should be closely monitored in all hepatitis C patients taking valproic acid. PMID: 12505820 [PubMed - indexed for MEDLINE]

5: Ann Intern Med 2002 Dec 17;137(12):961-4

Summary for patients in:

Ann Intern Med. 2002 Dec 17;137(12):I36.

Prevalence of liver disease in a population of asymptomatic persons with hepatitis C virus infection.

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BACKGROUND: The prevalence of significant liver disease in persons with

asymptomatic hepatitis C virus (HCV) infection is unclear. OBJECTIVE: To determine the prevalence and severity of HCV infection in asymptomatic persons. DESIGN: Population-based cross-sectional study. SETTING: Northeastern Italy. PATIENTS: 4820 apparently healthy Telecom Italy employees or their relatives who underwent screening for cardiovascular risk factors. MEASUREMENTS: Initial screening for anti-HCV by enzyme-linked immunosorbent assay followed by HCV RNA testing by polymerase chain reaction and monitoring of alanine aminotransferase levels in viremic persons (92% of viremic persons also had liver biopsies to assess their METAVIR scores). RESULTS: 116 persons (2.4% [95% CI, 1.97% to 2.84%]) were positive for anti-HCV and 85 (1.76% [CI, 1.39% to 2.14%]) were also viremic. The ALT level was persistently normal in 39 (46%) of viremic patients and elevated in 46 (54%). Significant hepatic histologic abnormalities were detected in 19% (CI, 7.21% to 36.4%) of persons with persistently normal ALT levels and in 61% (CI, 45.4% to 74.9%) of viremic persons who had elevated ALT levels ($P < 0.001$). The prevalence of HCV infection and number of persons with chronic liver fibrosis increased with age ($P = 0.003$). CONCLUSIONS: Hepatitis C is histologically active and progressive in up to 40% of asymptomatic persons with HCV infection. The severity of liver disease correlates with abnormal ALT levels and increases with age. PMID: 12484711 [PubMed - indexed for MEDLINE]

6: Arthritis Rheum 2002 Dec;46(12):3317-26

Interferon-alpha and ribavirin treatment in patients with hepatitis C virus-related systemic vasculitis.

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OBJECTIVE: Hepatitis C virus (HCV)-related vasculitis may involve multiple organs, including the skin, kidneys, and nervous system, and may be life-threatening. Although HCV is increasingly recognized as a cause of systemic vasculitis, limited data are available regarding the optimal treatment of this potentially serious condition. Therefore, we retrospectively analyzed the response to treatment in patients with chronic hepatitis C complicated by systemic vasculitis who had received antiviral therapy with interferon-alpha (IFNalpha) and ribavirin. METHODS: This retrospective study included 27 patients with systemic vasculitis and chronic HCV infection. Each patient had received treatment with IFNalpha and ribavirin for at least 6 months. The response to antiviral treatment was analyzed by comparing clinical, immunologic, and virologic data at the time of entry and during followup. Clinical response was defined according to the evolution of weight, arthralgia, nervous system, renal system, and cutaneous involvement. The virologic and immunologic responses were defined by the absence of HCV RNA and the absence of cryoglobulinemia, respectively, both 6 months after stopping antiviral therapy and at the end of followup. RESULTS: Patients received IFNalpha for a mean \pm SD of 20 \pm 14 months and ribavirin (at a mean \pm SD dosage of 895 \pm 250 mg/day) for 14 \pm 12 months. Other treatments included low-dose corticosteroids and plasma exchange. After a mean \pm SD followup of 57 \pm 29 months, 25 of 27 patients are alive and are being followed up as outpatients. Because of the heterogeneity of anti-HCV treatments received, the main results were stratified according to patients with 6 months of followup after stopping antiviral treatment (group 1, $n = 14$) and those who were still undergoing antiviral therapy at the time of analysis (group 2, $n = 13$). Nine patients in group 1 had a sustained virologic response and were clinical and immunologic complete responders. Four patients in group 1 were virologic nonresponders, and 3 of these patients had partial clinical and immunologic responses. Overall, 10 patients in group 1 had a complete clinical and immunologic response of their vasculitis (all 9 of the sustained virologic responders and 1 of the 5

patients who remained viremic). At the end of followup, 7 patients in group 2 were negative for HCV RNA; 6 were complete clinical responders. Among the other 6 patients in group 2, who had persistent viremia, 4 had a partial clinical response. Among the patients in group 1, HCV RNA was more often undetectable and genotype 1 was less frequent in complete clinical responders compared with partial/nonresponders. Age, sex, clinical vasculitic involvement, mean duration or total cumulative dose of IFNalpha or ribavirin, and use of steroids or plasmapheresis did not differ significantly according to clinical response. CONCLUSION: Treatment with IFNalpha and ribavirin can achieve a complete clinical response in most patients with HCV-related systemic vasculitis. Complete clinical response correlates with the eradication of HCV.

PMID: 12483738 [PubMed - indexed for MEDLINE]

7: Clin Immunol 2002 Dec;105(3):279-85

Serum concentration of gammaGT is a surrogate marker of hepatic TNF-alpha Mrna expression in chronic hepatitis C.

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Serum gammaGT levels and hepatic expression of tumor necrosis factor-alpha (TNF-alpha) are host factors that can independently predict the outcome of interferon (IFN) treatment in patients with chronic hepatitis C virus (HCV) infection. To explore whether a correlation exists between these two factors, we measured pretreatment gammaGT levels in serum and TNF-alpha mRNA levels in liver biopsies of chronic HCV patients. Seventy-two HCV patients treated with 3-to-5 million units of IFN-alpha three times a week were enrolled in the study. Treatment lasted 24 weeks and was followed by a 48-week follow-up period. Efficacy was assessed by measuring HCV RNA and alanine aminotransferase by the end of follow-up. Twelve patients (16.6%) showed a sustained biochemical and virological response. Normal pretreatment gammaGT levels, low HCV RNA titer, and infection with genotype other than HCV-1 were shown to be independent predictors of sustained response. Hepatic levels of TNF-alpha mRNA, quantified by polymerase chain reaction, were significantly higher in nonresponders (3.44 arbitrary units) compared to sustained responders (1.84 arbitrary units; $P = 0.009$). Values ≤ 3.12 arbitrary units independently predicted a sustained response to IFN ($P = 0.014$). Finally, TNF-alpha mRNA levels were significantly correlated with serum gammaGT levels ($r = 0.79$, $P < 0.0001$). These findings suggest that serum gammaGT levels may represent a surrogate marker of hepatic TNF-alpha expression, thus explaining the importance of serum gammaGT levels in predicting treatment outcome.

PMID: 12498809 [PubMed - indexed for MEDLINE]

8: Clin Infect Dis 2003 Jan 1;36(1):97-100

Hepatitis C virus and human immunodeficiency virus coinfection in an urban population: low eligibility for interferon treatment.

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One hundred eighty human immunodeficiency virus (HIV)- and hepatitis C virus (HCV)-coinfected patients were prospectively evaluated for suitability for interferon and ribavirin therapy. Of the 149 patients with chronic HCV infection who completed the evaluation, 44 (30%) were eligible for treatment and 105 (70%) were ineligible, with the main barriers being missed clinic visits, active psychiatric illness, active drug or alcohol use, decompensated liver disease, or medical illness.

PMID: 12491208 [PubMed - indexed for MEDLINE]

9: Dig Dis Sci 2002 Dec;47(12):2674-81

Assessment of fatigue in patients with chronic hepatitis C using the Fatigue Impact Scale.

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The aim of this study was to assess the impact of fatigue on the quality of life of patients with chronic hepatitis C (CHC) and to examine its relationship with various parameters of the disease, including viral load. The Fatigue Impact Scale (FIS), a self-report questionnaire, was applied to 92 patients with CHC, and the results were compared to those of an age-matched cohort of 213 healthy blood donors. Fatigue was frequent and disabling, being present in 67% of CHC patients, and the FIS was significantly increased in CHC patients compared to the healthy controls. Fatigue severity was not correlated with the activity of the disease or with the level of viremia. The FIS proved to be a valuable tool to assess this symptom. It should be of help for better evaluation of the clinical spectrum of the disease and should be included in trials assessing the efficacy of therapeutic interventions.

Publication Types:

Validation Studies

PMID: 12498284 [PubMed - indexed for MEDLINE]

10: Dig Dis Sci 2002 Dec;47(12):2686-90

Normalization of markedly elevated alpha-fetoprotein in a virologic nonresponder with HCV-related cirrhosis.

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Measurement of serum AFP can be useful in the diagnosis of hepatocellular carcinoma (HCC). AFP is a fetal protein that is not normally present in the serum of adults but is elevated in most patients with HCC. The diagnosis of HCC is generally made in patients with a mass lesion in a cirrhotic liver if the AFP is over 400 ng/ml. Unfortunately, AFP is elevated in other conditions such as nonseminomatous germ cell tumor, chronic hepatitis, cirrhosis, pregnancy, and hepatic metastasis. A high AFP cutoff value for HCC would increase the specificity of the test, but would decrease the sensitivity considerably. We report the case of a patient with HCV and cirrhosis with a markedly elevated AFP of 1257 ng/ml in whom no evidence of HCC could be found after a thorough radiologic and histologic evaluation. Despite a virologic nonresponse to IFN-alpha2b and ribavirin therapy, there was a complete normalization of AFP.

PMID: 12498286 [PubMed - indexed for MEDLINE]

11: Gastroenterology 2003 Jan;124(1):97-104

Progression of fibrosis in chronic hepatitis C.

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BACKGROUND & AIMS: Fibrosis is the hallmark of hepatic cirrhosis, worsening of which is probably the best surrogate marker for progression of chronic liver disease. We evaluated a large cohort of patients with chronic hepatitis C (CHC) using liver histology to assess the rate and predictors of progression of fibrosis. METHODS: The cohort consisted of 123 patients with CHC who underwent 2 liver biopsies 4-212 months (mean, 44 months) apart without intervening treatment. Liver histology was graded using the histology activity index (score, 0-18) and fibrosis staged using a scoring system of 0 (no fibrosis) to 6 (cirrhosis). RESULTS: Among 123 patients, 48

(39%) showed progression in fibrosis scores, 46 (37%) showed no change, and 29 (24%) showed improvement. Of those with worsening fibrosis, 75% had a 1-point increase and 25% a 2-point or greater increase in scores, and 9% showed progression to cirrhosis. The overall rate of progression was 0.12 fibrosis units per year, a rate that predicts progression to cirrhosis in 50 years if progression was linear. The rate of fibrosis progression was variable, and it was higher among older patients, those with higher serum alanine and aspartate aminotransferase levels, and those with the most extensive periportal necrosis on initial liver biopsy.

CONCLUSIONS: The best predictors of fibrosis progression in CHC are the extent of serum aminotransferase elevations and the degree of hepatocellular necrosis and inflammation on liver biopsy. These findings support the recommendation that patients with normal aminotransferase levels and mild liver histology can safely defer treatment.

PMID: 12512034 [PubMed - indexed for MEDLINE]

12: Hepatology 2003 Jan;37(1):65-71

Interleukin-1beta gene polymorphisms associated with hepatocellular carcinoma in hepatitis C virus infection.

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Hepatitis C virus (HCV) infection is a major risk factor for developing hepatocellular carcinoma (HCC), a life-threatening sequel. However, the factors that affect disease progression to HCC have not been thoroughly elucidated. Genetic polymorphisms in proinflammatory cytokines, the interleukin 1 (IL-1) family (IL-1beta and IL-1ra) and tumor necrosis factor-alpha (TNF-alpha), were studied in 274 Japanese patients with chronic HCV infection and 55 healthy individuals using standard polymerase chain reaction-based genotyping techniques. The association between these polymorphisms and disease status was evaluated while controlling for confounding clinical variables. The proportion of patients with HCC in the IL-1beta-31 T/T (55%, odds ratio to C/C was 2.63, $P = .009$) genotype was higher than in the T/C (44%, odds ratio to C/C was 1.64, $P = .149$) and C/C genotypes (35%). The IL-1beta-31 and -511 loci were in near complete linkage disequilibrium, and the IL-1beta-511/-31 haplotype C-T was significantly associated with the presence of HCC (odds ratio of 1.51, $P = .02$). Polymorphisms in the TNF-alpha gene were not associated with disease. A multivariate analysis revealed that the IL-1beta-31 T/T genotype, alpha-fetoprotein >20 microg/L, presence of cirrhosis, male sex, and age >60 years were associated with the presence of HCC at odds ratios of 3.73 (T/T vs. C/C), 4.12, 4.03, 3.89, and 3.27, respectively. In conclusion, the IL-1beta-31 genotype T/T or the IL-1beta-511/-31 haplotype C-T is associated with the presence of HCC in Japanese patients with chronic HCV infection.

PMID: 12500190 [PubMed - indexed for MEDLINE]

13: Hepatology 2003 Jan;37(1):60-4

Spontaneous viral clearance in patients with acute hepatitis C can be predicted by repeated measurements of serum viral load.

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Early interferon (IFN) therapy prevents viral persistence in acute hepatitis C, but in view of the resulting costs and morbidity patients who really need therapy have to be identified. Twelve consecutive patients with acute hepatitis C (9 women, 3 men, mean age: 39.5 +/- 18.8 y, genotype 1: 7, genotype 3a: 3, 2 could not be

genotyped) were studied. The sources of infection were medical procedures in 6, sexual transmission in 3, and intravenous drug abuse in 3 patients. Viral load was measured by Cobas Amplicor HCV Monitor v2.0 (Roche Diagnostic Systems, Branchburg, NY). The time from infection to clinical symptoms was 43.3 +/- 8.6 (mean +/- SD) days. Eight patients cleared hepatitis C virus (HCV) spontaneously and remained HCV-RNA negative with a follow-up of 9.0 +/- 3.9 months. In these patients viral load declined fast and continuously. The time from exposure to HCV-RNA negativity was 77.4 +/- 25.3 and from the first symptoms was 34.7 +/- 22.1 days. In 4 patients HCV-RNA levels remained high or even increased. Two of them became sustained responders to treatment initiated after a 6-week observation period. The 2 remaining patients were not treated (one because of contraindications for IFN, the other declined therapy) and are still HCV-RNA positive. In conclusion, patients with acute icteric hepatitis C have a high rate of spontaneous viral clearance within the first month after the onset of symptoms. IFN therapy appears only needed in patients who fail to clear the virus within 35 days after onset of symptoms. By this approach, IFN therapy was not necessary in two thirds of patients with acute hepatitis C.

Publication Types:

Multicenter Study

PMID: 12500189 [PubMed - indexed for MEDLINE]

14: Isr Med Assoc J 2002 Dec;4(12):1101-5

True primary Sjogren's syndrome in a subset of patients with hepatitis C infection: a model linking chronic infection to chronic sialadenitis.

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BACKGROUND: Hepatitis C virus infection is presently an exclusion criterion to classify Sjogren's syndrome; however, there are distinct clinicopathologic and biologic similarities between HCV-related and SS-related chronic inflammation of mucosa-associated lymphoid tissue and lymphoproliferation that suggest common pathogenetic pathways. **OBJECTIVES:** To determine whether a subset of patients with sicca syndrome and HCV infection may present a true primary SS rather than a distinct clinicobiologic entity. **METHODS:** We extensively characterized 20 consecutive patients with positive anti-HCV antibodies and heavy subjective dry eye and/or dry mouth symptoms, plus positive unstimulated sialometry and/or Shirmer's test. We then compared these features with those in HCV-negative primary SS controls (classified according to the latest American-European Consensus Group Classification Criteria for SS). **RESULTS:** Of the 20 HCV-positive patients with sicca manifestations, 12 (60%) had positive anti-SSA/SSB antibodies (3/12 by enzyme-linked immunosorbent assay and 6/12 by immunoblot) and/or positive salivary gland biopsy (at least 1 focus/4 mm²), which met the strict classification criteria for SS, as in the case of HCV-negative SS controls. Comparing the HCV-positive SS subset with HCV-negative SS controls showed similar female to male ratio (11/1 vs. 46/4), major salivary gland swelling (17% vs. 26%), positive antinuclear antibodies (75 vs. 94%) and positive rheumatoid factor (58 vs. 52%). Significant differences ($P < 0.05$) were seen in mean age (69 vs. 56 years), liver disease (50 vs. 2%), lung disease (25 vs. 0%), anti-SSA/SSB positivity (25 vs. 90%), and low C3 or C4 (83 vs. 36%). HCV-positive SS patients exhibited a trend for more frequent chronic gastritis 50 vs. 22%), fibromyalgia (33 vs. 14%), peripheral neuropathy (33 vs. 18%), purpura (33 vs. 19%) and cryoglobulinemia (33 vs. 6%). **CONCLUSIONS:** A major subset of HCV-positive patients with definite subjective sicca symptoms and positive objective tests may indeed present a true, though peculiar, subset of SS. There are strict similarities with key clinical, pathologic and immunologic findings of definite HCV-negative SS. Other features appear more characteristic of HCV infection. When also considering

that HCV is sialotropic and may be treated, HCV-related chronic sialadenitis represents a unique opportunity to clarify key pathogenetic events occurring in the large majority of HCV-negative SS; and similarities to typical primary SS, rather than differences, should be taken into account.
PMID: 12516900 [PubMed - indexed for MEDLINE]

15: Muscle Nerve 2003 Jan;27(1):102-4

Viral RNA in nerve tissues of patients with hepatitis C infection and peripheral neuropathy.

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To assess the presence of viral ribonucleic acid (RNA) in nerve tissues of 15 patients with hepatitis C virus (HCV) infection and peripheral neuropathy with (11) or without (4) mixed cryoglobulinemia, nested reverse transcription-polymerase chain reaction (RT-PCR) was performed. Amplification of HCV-RNA was successful in 7 patients with and 3 without mixed cryoglobulinemia. This study demonstrates that the nested RT-PCR technique is a sensitive method to detect viral RNA in nerve tissue, and offers further evidence that in patients with HCV infection peripheral neuropathy can occur in the absence of mixed cryoglobulinemia.

PMID: 12508302 [PubMed - indexed for MEDLINE]

16: Nat Rev Immunol 2003 Jan;3(1):51-62

Hepatic T cells and liver tolerance.

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The T-cell biology of the liver is unlike that of any other organ. The local lymphocyte population is enriched in natural killer (NK) and NKT cells, which might have crucial roles in the recruitment of circulating T cells. A large macrophage population and the efficient trafficking of dendritic cells from sinusoidal blood to lymph promote antigen trapping and T-cell priming, but the local presentation of antigen causes T-cell inactivation, tolerance and apoptosis. These local mechanisms might result from the need to maintain immunological silence to harmless antigenic material in food. The overall bias of intrahepatic T-cell responses towards tolerance might account for the survival of liver allografts and for the persistence of some liver pathogens.

Publication Types:

Review

Review, Tutorial

PMID: 12511875 [PubMed - indexed for MEDLINE]

17: Pediatrics 2003 Jan;111(1):153-7

Prevalence of hepatitis C virus infection and risk factors in an incarcerated juvenile population: a pilot study.

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OBJECTIVE: Hepatitis C virus (HCV) infection is the leading cause of liver failure in adulthood. Although the prevalence of HCV is reportedly as high as 80% in incarcerated adult populations, little is known about the prevalence of HCV in incarcerated juvenile populations. The purpose of this study was to determine the prevalence of HCV and high-risk behaviors in a population of incarcerated youths.

METHODS: We conducted a cross-sectional prevalence study of HCV infection in youths who were admitted to a juvenile detention center between September 1999 and January 2001. Subjects were asked questions regarding behaviors that might put them at risk for acquiring HCV, and blood was drawn for HCV antibody testing. Qualitative HCV RNA testing was performed on antibody-positive subjects. **RESULTS:** Seventy-four percent (n = 305) of youths consented to participate in the seroprevalence study. HCV risk behaviors were common in this population: sexual activity (70%), intravenous drug use (6%), intranasal drug use (32%), body piercing (53%), and tattoos (33%). Six study youths (2%) were HCV antibody positive; 4 of these subjects were also HCV RNA positive. HCV-positive status was significantly associated with history of intravenous drug use and having had a sexually transmitted disease. Only 17% of study participants could correctly identify behaviors that might put them at risk for HCV. **CONCLUSIONS:** The prevalence of HCV in incarcerated youths is higher than in the general pediatric population but not yet at adult levels of prevalence. Given the high prevalence of risk factors in this population, future studies should address the need for targeted HCV screening and education of incarcerated youths regarding risks for HCV. PMID: 12509569 [PubMed - indexed for MEDLINE]